WHAT IS CLAIMED IS:

1. A method for obtaining a bioactivity or a biomolecule of interest, comprising:

a) screening a library of clones generated from nucleic acids from a mixed population of cells, for a specified bioactivity or biomolecule;

b) variegating a nucleic acid sequence contained in a clone having the specified bioactivity or biomolecule; and

c) comparing the bioactivity or biomolecule from b) with the specified bioactivity or biomolecule wherein a difference in the bioactivity or biomolecule is indicative of an effect of sequence variegation, thereby providing the bioactivity or biomolecule of interest.

2. The method of claim 1, wherein the biomolecule is a nucleic acid sequence.

3. The method of claim 2, wherein the nucleic acid sequence is a DNA or RNA sequence.

4. The method of claim 2, wherein the nucleic acid sequence is screened by contacting the nucleic acids contained in the clone with at least one oligonucleotide probe comprising a detectable molecule and at least a portion of the nucleic acid sequence of interest; and

identifying nucleic acid sequences containing a complement to the at least one oligonucleotide probe with an analyzer that detects a detectable signal from the detectable molecule.

5. The method of claim 4, wherein the detectable molecule is a chromogenic or a fluorogenic substrate.

6. The method of claim 4, wherein the detectable signal is optical fluorescence.

7. The method of claim 5, wherein the fluorogenic substrate is umbelliferone or a derivative or analogue thereof, resorufin or a derivative or analogue thereof,

fluorescein or a derivative or analogue thereof, or rhodamine or a derivative or analogue thereof.

8. The method of claim 4, wherein the detectable molecule is a detectably labeled oligonucleotide having a sequence encoding a polypeptide of interest or a fragment thereof.

9. The method of claim 8, wherein the detectably labeled oligonucleotide is labeled with a fluorescent molecule.

10. The method of claim 2, wherein the screening is by PCR amplification of a nucleic acid sequence of interest using primers substantially complementary to the sequence of interest or sequences flanking a nucleic acid of interest and having a detectable molecule.

11. The method of claim 2, wherein the screening is by hybridization of an oligonucleotide substantially complementary to a nucleic acid sequence of interest and having a detectable molecule.

12. The method of claim 2, further comprising comparing the variegated nucleic acid sequence of interest to the non-variegated nucleic acid sequence of (c), thereby identifying the nucleotide sequence variegation.

13. The method of claim 12, wherein the comparison is performed using a sequence comparison algorithm.

14. The method of claim 1, wherein the bioactivity is provided by a polypeptide.

15. The method of claim 1, wherein the bioactivity is an enzymatic activity.

16. The method of claim 15, wherein the enzymatic activity is provided by an enzyme selected from the group consisting of lipases, esterases, proteases, glycosidases,

glycosyl transferases, phosphatases, kinases, mono- and dioxygenases, haloperoxidases, lignin peroxidases, diarylpropane peroxidases, epozide hydrolases, nitrile hydratases, nitrilases, transaminases, amidases, and acylases.

17. The method of claim 1, wherein the library is an expression library.

18. The method of claim 1, wherein the library contains DNA obtained from an environmental sample.

19. The method of claim 1, wherein the library contains DNA obtained from extremophiles.

20. The method of claim 19, wherein the extremophiles are thermophiles.

21. The method of claim 20, wherein the extremeophiles are selected from the group consisting of hyperthermophiles, psychrophiles, halophiles, psychrotrophs, alkalophiles, and acidophiles.

22. The method of claim 17, wherein the screening comprises contacting a clone with a substrate labeled with a detectable molecule wherein interaction of the substrate with the bioactivity or biomolecule contained in the clone produces a detectable signal.

23. The method of claim 22, wherein the substrate is a bioactive substrate.

24. The method of claim 22, wherein the bioactive substrate comprises C12FDG.

25. The method of claim 22, wherein the substrate comprises a first test protein linked to a DNA binding moiety and a second test protein linked to a transcriptional activation moiety, wherein modulation of the interaction of the first test protein linked to the DNA binding moiety with the second test protein linked to the transcription activation moiety results in a change in the expression of a detectable protein.

26. The method of claim 22, wherein the screening is by expression of nucleic acid.

27. The method of claim 1, further comprising, prior to (d), obtaining nucleic acids from the clone containing the specified bioactivity or biomolecule.

28. The method of claim 27, wherein obtaining the nucleic acids contained in the clone comprises contacting the clone with a complementary nucleic acid, or fragment thereof, thereby allowing hybridization of the clone nucleic acids with the complementary nucleic acid and isolation thereof.

29. The method of claim 28, wherein the complementary nucleic acid or fragment thereof comprises a solid phase bound hybridization probe.

30. The method of claim 1, wherein the nucleic acid sequence is variegated by a method selected from the group consisting of error-prone PCR, shuffling, oligonucleotide-directed mutagenesis, assembly PCR, sexual PCR mutagenesis, *in vivo* mutagenesis, cassette mutagenesis, recursive ensemble mutagenesis, exponential ensemble mutagenesis, site-specific mutagenesis, ligation reassembly, GSSM and any combination thereof.

31. The method of claim 1, wherein the nucleic acid sequence is variegated by error-prone PCR.

32. The method of claim 1, wherein the nucleic acid sequence is variegated by shuffling.

33. The method of claim 1, wherein the nucleic acid sequence is variegated by oligonucleotide-directed mutagenesis.

34. The method of claim 1, wherein the nucleic acid sequence is variegated by assembly PCR.

35. The method of claim 1, wherein the nucleic acid sequence is variegated by sexual PCR mutagenesis.

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36. The method of claim 1, wherein the nucleic acid sequence is variegated by *in vivo* mutagenesis.

37. The method of claim 1, wherein the nucleic acid sequence is variegated by cassette mutagenesis.

38. The method of claim 1, wherein the nucleic acid sequence is variegated by recursive ensemble mutagenesis.

39. The method of claim 1, wherein the nucleic acid sequence is variegated by exponential ensemble mutagenesis.

40. The method of claim 1, wherein the nucleic acid sequence is variegated by site-specific mutagenesis.

41. The method of claim 1, comprising screening the clone of (c) for a further specified protein or enzymatic activity, prior to variegating the nucleic acids.

42. The method of claim 1, wherein the library is generated in a prokaryotic cell.

43. The method of claim 1, wherein the library is generated in a *Streptomyces sp.*

44. The method of claim 43, wherein the Streptomyces is *Streptomyces venezuelae.*

45. The method of claim 42, wherein the prokaryotic cell is gram negative.

46. The method of claim 42, wherein the prokaryotic cell is a *Bacillus sp.*

47. The method of claim 42, wherein the prokaryotic cell is a *Pseudomonas sp.*

48. The method of claim 1, wherein the library is screened by contacting or encapsulating a clone of the library with bioactive substrate, wherein a bioactivity or biomolecule produced by the clone is detectable by a difference in the substrate prior to contacting with the clone as compared to after contacting.

49. The method of claim 1, wherein the library is normalized before screening the library.

50. The method of claim 1, wherein the bioactivity or biomolecule is a gene cluster or fragment thereof.

51. The method of claim 1, wherein the bioactivity or biomolecule is a polypeptide in a metabolic pathway.

52. A method for identifying a bioactivity or a biomolecule of interest, comprising:

a) screening a library of clones generated from pooled nucleic acids obtained from a plurality of isolates for a specified bioactivity or biomolecule; and

b) identifying a clone which contains the specified bioactivity or biomolecule.

53. A method for identifying a bioactivity or a biomolecule of interest, comprising:

a) screening a library of clones generated from pooled nucleic acids obtained from a plurality of isolates for a specified bioactivity or biomolecule;

b) variegating a nucleic acid sequence contained in a clone having the specified bioactivity or biomolecule; and

c) comparing the bioactivity or biomolecule from b) with the specified bioactivity or biomolecule wherein a difference in the bioactivity or biomolecule is indicative of an effect of introducing at least one sequence variegation, thereby providing the bioactivity or biomolecule of interest.

54. A method for identifying a bioactivity or a biomolecule of interest, comprising:

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a) screening a library of clones generated from pooling individual gene libraries generated from the nucleic acids obtained from each of a plurality of isolates for a specified bioactivity or biomolecule; and

b) identifying a clone which contains the specified bioactivity or biomolecule.

55. A method for identifying a bioactivity or a biomolecule of interest, comprising:

a) screening a library for a specified bioactivity or biomolecule wherein the library is generated from pooling individual gene libraries generated from the nucleic acids obtained from each of a plurality of isolates;

b) variegating a nucleic acid sequence contained in a clone having the specified bioactivity or biomolecule; and

c) comparing the bioactivity or biomolecule from c) with the specified bioactivity or biomolecule wherein a difference in the bioactivity or biomolecule is indicative of an effect of introducing at least one sequence variegation, thereby providing the bioactivity or biomolecule of interest.

56. A method of identifying a bioactivity or biomolecule of interest, comprising:

(a) screening a library of clones generated from the nucleic acids from an enriched population of organisms for a specified bioactivity or biomolecule; and

(b) identifying a clone containing the specified bioactivity or biomolecule.

57. A method of identifying a bioactivity or biomolecule of interest, comprising:

(a) screening a library of clones generated from nucleic acids from an enriched population of organisms for a specified bioactivity or biomolecule;

(b) variegating a nucleic acid sequence contained in a clone having the specified bioactivity or biomolecule; and

(c) comparing the bioactivity or biomolecule from b) with the specified bioactivity or biomolecule wherein a difference in the bioactivity or biomolecule is indicative of an effect of introducing at least one sequence variegation, thereby providing the bioactivity or biomolecule of interest.

58. A method for identifying a bioactivity or a biomolecule of interest, comprising:

(a) incubating nucleic acids from a mixed population of organisms with at least one oligonucleotide probe comprising a detectable molecule and at least a portion of a nucleic acid sequence encoding a molecule of interest under such conditions and such time to allow interaction of complementary sequences;

(b) identifying nucleic acid sequences having a complement to the oligonucleotide probe using an analyzer that detects the detectable molecule;

(c) generating a library from the identified nucleic acid sequences;

(d) screening the library for a specified bioactivity or biomolecule;

(e) variegating a nucleic acid sequence contained in a clone having the specified bioactivity or biomolecule; and

(f) comparing the bioactivity or biomolecule product from (e) with the specified bioactivity or biomolecule wherein a difference in the bioactivity or biomolecule is indicative of an effect of introducing at least one sequence variation, thereby providing the bioactivity or biomolecule of interest

59. A method for identifying a bioactivity or a biomolecule of interest, comprising:

(a) co-encapsulating in a microenvironment nucleic acids obtained from a mixed population of organisms, with at least one oligonucleotide probe comprising a detectable molecule and at least a portion of a nucleic acid sequence encoding a molecule of interest under such conditions and for such time as to allow interaction of complementary sequences;

(b) identifying encapsulated nucleic acids containing a complement to the oligonucleotide probe encoding the molecule of interest by separating the encapsulated nucleic acids with an analyzer that detects the detectable molecule;

(c) generating a library from the separated encapsulated nucleic acids;

(d) screening the library for a specified bioactivity or biomolecule;

(e) variegating a nucleic acid sequence contained in a clone having the specified bioactivity or biomolecule; and

(f) comparing the bioactivity or biomolecule product from (e) with the specified bioactivity or biomolecule wherein a difference in the bioactivity or

biomolecule is indicative of an effect of introducing at least one sequence variation, thereby providing the bioactivity or biomolecule of interest.

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60. A method for identifying a bioactivity or a biomolecule of interest, comprising:

(a) co-encapsulating in a microenvironment nucleic acids obtained from an isolate of a mixed population of organisms, with at least one oligonucleotide probe comprising a detectable marker and at least a portion of a polynucleotide sequence encoding a molecule having a bioactivity of interest under such conditions and for such time as to allow interaction of complementary sequences;

(b) identifying encapsulated nucleic acids containing a complement to the oligonucleotide probe encoding the molecule of interest by separating the encapsulated nucleic acids with an analyzer that detects the detectable marker;

(c) generating a library from the separated encapsulated nucleic acids;

(d) screening the library for a specified bioactivity or biomolecule;

(e) variegating a nucleic acid sequence contained in a clone having the specified bioactivity or biomolecule; and

(f) comparing the bioactivity or biomolecule product from (e) with the specified bioactivity or biomolecule wherein a difference in the bioactivity or biomolecule is indicative of an effect of introducing at least one sequence variation, thereby providing the bioactivity or biomolecule of interest.

61. A method for obtaining a bioactivity or a biomolecule of interest, comprising:

(a) co-encapsulating in a microenvironment nucleic acids obtained from one or more isolates of a mixed population of organisms, with at least one oligonucleotide probe comprising a detectable marker and at least a portion of a polynucleotide sequence encoding a molecule having a bioactivity of interest under such conditions and for such time as to allow interaction of complementary sequences;

(b) identifying encapsulated nucleic acids containing a complement to the oligonucleotide probe encoding the molecule of interest by separating the encapsulated nucleic acids with an analyzer that detects the detectable marker;

(c) generating a library from the separated encapsulated nucleic acids;

(d) screening the library for a specified bioactivity or biomolecule;

(e) variegating a nucleic acid sequence contained in a clone having the specified bioactivity or biomolecule; and

(f) comparing the bioactivity or biomolecule product from (e) with the specified bioactivity or biomolecule wherein a difference in the bioactivity or biomolecule is indicative of an effect of introducing at least one sequence variation, thereby providing the bioactivity or biomolecule of interest.

62. A method for identifying a bioactivity or a biomolecule of interest, comprising:

(a) co-encapsulating in a microenvironment nucleic acids obtained from a mixture of isolates of a mixed population of organisms, with at least one oligonucleotide probe comprising a detectable marker and at least a portion of a polynucleotide sequence encoding a molecule having a bioactivity of interest under such conditions and for such time as to allow interaction of complementary sequences;

(b) identifying encapsulated nucleic acids containing a complement to the oligonucleotide probe encoding the molecule of interest by separating the encapsulated nucleic acids with an analyzer that detects the detectable marker;

(c) generating a library from the separated encapsulated nucleic acids;

(d) screening the library for a specified bioactivity or biomolecule;

(e) variegating the a nucleic acid sequence contained in a clone having the specified bioactivity or biomolecule; and

(f) comparing the bioactivity or biomolecule product from (e) with the specified bioactivity or biomolecule wherein a difference in the bioactivity or biomolecule is indicative of an effect of introducing at least one sequence variation, thereby providing the bioactivity or biomolecule of interest.